AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

33. (Currently amended) A method for reducing colonization of ~~enterohemorragic~~ enterohemorrhagic *Escherichia coli* (EHEC) in a non-human mammal comprising administering to said ~~ruminant a therapeutically~~ non-human mammal an effective amount of a composition comprising an EHEC cell culture supernatant.

34. (Currently amended) A method for reducing shedding of ~~enterohemorragic~~ enterohemorrhagic *Escherichia coli* (EHEC) from a non-human mammal comprising administering to said ~~ruminant a therapeutically~~ non-human mammal an effective amount of a composition comprising an EHEC cell culture supernatant.

35. (Currently amended) The method of claim 33, wherein the non-human mammal is a ruminant.

36. (Previously presented) The method of claim 35, wherein the ruminant is a bovine subject.

37. (Previously presented) The method of claim 33, wherein the composition further comprises an immunological adjuvant.

38. (Previously presented) The method of claim 33, wherein the EHEC is EHEC O157:H7.

39. (Previously presented) The method of claim 33, wherein the EHEC is EHEC O157:NM.

40. (Previously presented) The method of claim 37, wherein the immunological adjuvant

comprises an oil-in-water emulsion.

41. (Currently amended) The method of claim ~~40~~37, wherein the immunological adjuvant comprises a mineral oil and dimethyldioctadecylammonium bromide.

42. (Currently amended) The method of claim ~~41~~37, wherein the immunological adjuvant ~~is~~ ~~VSA3~~ comprises a non-oil-in-water emulsion.

43. (Currently amended) The method of claim ~~42~~37, wherein the ~~VSA3~~ immunological adjuvant is present in the composition at a concentration of ~~about~~ 20% to ~~about~~ 40% (v/v).

44. (Currently amended) The method of claim 43, wherein the ~~VSA3~~ immunological adjuvant is present in the composition at a concentration of ~~about~~ 30% (v/v).

45. (Previously presented) The method of claim 33, wherein the composition further comprises one or more recombinant or purified EHEC antigens selected from the group consisting of EspA, EspB, EspD, Tir and Intimin.

46. (Currently amended) The method of claim 45, wherein EspA+Tir comprise ~~at least 20%~~ 10% to 50% of the cell protein present in the composition.

47. (Previously presented) The method of claim 37, wherein the composition further comprises one or more recombinant or purified EHEC antigens selected from the group consisting of EspA, EspB, EspD, Tir and Intimin.

48. (Currently amended) The method of claim 47, wherein EspA+Tir comprise ~~at least 20%~~ 10% to 50% of the cell protein present in the composition.

49. (Currently amended) The method of claim 34, wherein the non-human mammal is a ruminant.

50. (Previously presented) The method of claim 49, wherein the ruminant is a bovine subject.

51. (Previously presented) The method of claim 34, wherein the composition further comprises an immunological adjuvant.

52. (Previously presented) The method of claim 34, wherein the EHEC is EHEC O157:H7.

53. (Previously presented) The method of claim 34, wherein the EHEC is EHEC O157:NM.

54. (Previously presented) The method of claim 51, wherein the immunological adjuvant comprises an oil-in-water emulsion.

55. (Currently amended) The method of claim ~~54~~51, wherein the immunological adjuvant comprises a mineral oil and dimethyldioctadecylammonium bromide.

56. (Currently amended) The method of claim ~~55~~51, wherein the immunological adjuvant ~~is VSA3~~ comprises a non-oil-in-water emulsion.

57. (Currently amended) The method of claim ~~56~~51, wherein ~~VSA3~~ the immunological adjuvant is present in the composition at a concentration of ~~about~~ 20% to ~~about~~ 40% (v/v).

58. (Currently amended) The method of claim ~~57~~51, wherein ~~VSA3~~ the immunological adjuvant is present in the composition at a concentration of ~~about~~ 30% (v/v).

59. (Previously presented) The method of claim 34, wherein the composition further

comprises one or more recombinant or purified EHEC antigens selected from the group consisting of EspA, EspB, EspD, Tir and Intimin.

60. (Currently amended) The method of claim 59, wherein EspA+Tir comprise ~~at least 20%~~ 10% to 50% of the cell protein present in the composition.

61. (Previously presented) The method of claim 51, wherein the composition further comprises one or more recombinant or purified EHEC antigens selected from the group consisting of EspA, EspB, EspD, Tir and Intimin.

62. (Currently amended) The method of claim 61, wherein EspA+Tir comprise ~~at least 20%~~ 10% to 50% of the cell protein present in the composition.

63. (New) The method of claim 37 or 51, wherein the immunological adjuvant comprises an agent selected from the group consisting of an emulsifying agent, a muramyl dipeptide, an aqueous agent, a chitosan-based agent, a saponin, an oil, a lipopolysaccharide, a bacterial cell wall extract, a bacterial DNA, a bacterial complex, a synthetic oligonucleotide, and a aliphatic nitrogenous base.

64. (New) The method of claim 63, wherein the emulsifying agent is selected from the group consisting of a natural emulsifying agent, a synthetic emulsifying agent, an anionic emulsifying agent, a cationic emulsifying agent, and a nonionic agent.

65. (New) The method of claim 64, wherein the natural emulsifying agent is selected from the group consisting of acacia, gelatin, lecithin, and cholesterol.

66. (New) The method of claim 64, wherein the anionic emulsifying agent is selected from the group consisting of a potassium salt of lauric acid, a potassium salt of oleic acid, a sodium

salt of lauric acid, a sodium salt of oleic acid, an ammonium salt of lauric acid, an ammonium salt of oleic acid, a calcium salt of a fatty acid, a magnesium salt of a fatty acid, an aluminum salt of a fatty acid, a metallic soap, and an organic sulfonate.

67. (New) The method of claim 66, wherein the organic sulfonate is sodium lauryl sulfate.

68. (New) The method of claim 64, wherein the cationic emulsifying agent is cetyltrimethylammonium bromide.

69. (New) The method of claim 64, wherein the synthetic nonionic agent is selected from the group consisting of a glyceryl ester, a polyoxyethylene glycol ester, a polyoxyethylene glycol ether, and a sorbitan fatty acid ester.

70. (New) The method of claim 69, wherein the glyceryl ester is glyceryl monostearate.

71. (New) The method of claim 69, wherein the sorbitan fatty acid ester is selected from the group consisting of a sorbitan monopalmitate and polyoxyethylene derivatives thereof.

72. (New) The method of claim 69, wherein the polyoxyethylene derivatives is polyoxyethylene sorbitan monopalmitate.

73. (New) The method of claim 63, wherein the aqueous agent is aluminum hydroxide.

74. (New) The method of claim 63, wherein the oil is selected from the group consisting of a mineral oil, a vegetable oil, and an animal oil.

75. (New) The method of claim 74, wherein the vegetable oil is selected from the group consisting of canola oil, almond oil, cottonseed oil, corn oil, olive oil, peanut oil, safflower oil,

sesame oil, and soybean oil.

76. (New) The method of claim 74, wherein the animal oil is selected from the group consisting of cod liver oil, halibut oil, menhaden oil, orange roughy oil and shark liver oil.

77. (New) The method of claim 37 or 51, wherein the immunological adjuvant comprises an oil component.

78. (New) The method of claim 77, wherein the oil component is selected from the group consisting of a single oil, and a mixture of oils.

79. (New) The method of claim 42 or 56, wherein the non-oil-in-water emulsion is selected from the group consisting of an oil emulsion, a water-in-oil emulsion, and a water-in-oil-in-water emulsion.

80. (New) The method of claim 40 or 54, wherein the oil-in-water emulsion is EMULSIGEN PLUS^{TM}, i.e., an emulsion comprising a light mineral oil having 0.05% formalin and 30 mg/ml gentamycin.

81. (New) The method of claim 40 or 54, wherein the oil-in-water emulsion is VSA3.

82. (New) The method of claim 63, wherein the oil is Amphigen.

83. (New) The method of claim 37 or 51, wherein the immunological adjuvant comprises Mycobacterial cell wall extract.

84. (New) The method of claim 37 or 51, wherein the immunological adjuvant comprises Mycobacterial DNA.

85. (New) The method of claim 37 or 51, wherein the immunological adjuvant comprises a Mycobacterial cell wall complex.

86. (New) The method of claim 63, wherein the aliphatic nitrogenous base is selected from the group consisting of an amine, a quaternary ammonium compound, a guanidine, a benzamidine, and a thiouronium.

87. (New) The method of claim 37 or 51, wherein the immunological adjuvant comprisesdimethyl-dioctadecylammonium bromide.

88. (New) The method of claim 63, wherein the aliphatic nitrogenous base is N,N-dioctadecyl-N,N-bis(2-hydroxyethyl)propanediamine.

89. (New) The method of claim 46, 48, 60, or 62, wherein EspA+Tir comprise 20% of the cell protein present in the composition.

90. (New) The method of claim 35 or 49, wherein the ruminant is an ovine subject.

REMARKS

Claims 33-62 are pending. By the present amendment, claims 33-35, 41-44, 46, 48, 49, 55-58, 60, and 62 are amended, and new claims 63-90 are added.

Amendments

The specification has been amended to delete "(Zacek D. Animal Health and Veterinary Vaccines, Alberta Research Counsel, Edmonton, Canada, 1997)" in paragraph [0006], as this citation was included in error.

Support for the amendment reciting "non-human" mammal in claims 33 and 34 may be found in the specification at, for example, paragraph [0075] which describes a cell culture supernatant from a mutated EHEC having reduced toxicity for use in humans and clearly contemplates alternative compositions for use in non-human mammals and in humans.

New claims 63-89 have been added, and claims 42 and 56 have been amended, to recite various groups of immunological adjuvants. Support for this amendment may be found for example at paragraphs [0092] through [0094] of the published U.S. patent application, or at pp. 20-22 of the filed application. New claim 90 has been added to recite an ovine subject (see for example paragraph [0071] and Example 12).

The claims have also been amended to correct typographical errors.

No new matter has been added by the amendments.

Specification

The Examiner objected to use of the term "VSA3" as being a trademark that had not been identified as such in the application, and requested appropriate correction. This objection is respectfully traversed. It is the applicant's understanding that the term VSA3 refers to an adjuvant formulation containing emulsion and dimethyldioctadecyl ammonium bromide (DDA) (see, for example, U.S. Patent 5,951,988 issued to Little-van den Hurk et al.) and is not a trademark. Accordingly, the applicant respectfully submits that the term "VSA3" does not require correction.

Rejections Under 35 U.S.C. § 112

Claims 33-62 are rejected under 35 U.S.C. § 112, first paragraph, based on the assertion that the specification does not enable a skilled person to make and/or use the invention commensurate in scope with the claims. More specifically, while the Examiner concedes that the specification enables methods of reducing colonization or shedding of enterohemorrhagic *Escherichia coli* (hereafter "EHEC") in bovine and ovine species, the Examiner asserts that the specification does not enable methods of reducing colonization or shedding of EHEC in all mammals including humans. In support of this assertion, the Examiner further asserts that it is "well known in the art that ... cattle are ... carriers of EHEC while in humans EHEC is an important pathogen causing diarrhea with life threatening complications." The Examiner also addresses the "*Wands* factors" as set out in the MPEP 2164.01(a) and asserts that 1) there is insufficient direction or guidance presented in the specification with respect to methods of reducing colonization or generating protective responses in all mammals, 2) there are no working examples which suggest the desired result of protecting against EHEC, 3) the nature of the invention involves the complex and incompletely understood area of protective immune responses against EHEC, 4) the state of the prior art shows the lack of correlates to immunity with EHEC specially in humans, and that 5) the relative skill of those in the art is high.

Claims 33 and 34, as presently amended, are directed to methods of reducing colonization or shedding, respectively, of EHEC in a non-human mammal by administering an effective amount of a composition including an EHEC cell culture supernatant, and are the only pending independent claims. Accordingly, the enablement rejection will first be addressed with respect to claims 33 and 34.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation; the fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation (MPEP 2164.01). The MPEP also states that the "amount of guidance or direction needed to enable the invention is inversely

related to the amount of knowledge in the state of the art as well as the predictability in the art ... The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention" (MPEP 2164.03).

With respect to the Examiner's assertions that the nature of the invention involves the complex and incompletely understood area of protective immune responses against EHEC and that the state of the prior art shows the lack of correlates to immunity with EHEC specially in humans, the applicants respectfully submit that the Examiner has not provided evidence or reasoning to back these assertions, as is required (MPEP 2164.04). The initial burden lies on the Examiner to establish a reasonable basis to question the enablement provided for the claimed invention and to provide a reason for doubting the objective truth of the statements in the specification (MPEP 2164.04) and the applicant respectfully submits that this burden has not been met in the present case.

In the present case, the claims as amended are directed to methods of reducing colonization or shedding of EHEC in a non-human mammal by administering an effective amount of an EHEC cell culture supernatant. The specification teaches that compositions according to the invention may be administered to non-human mammals to reduce shedding or colonization of EHEC (see, for example, paragraphs [0073] and [0074]). The specification also provides detailed guidance for preparing and administering such compositions (see, for example, paragraphs [0078] to [0103] and Example 1) and for assaying shedding and colonization (see, for example, Example 6). In addition, the specification provides working examples of reducing shedding and colonization of EHEC by administration of the compositions of the invention to different groups of cattle and to sheep (see, for example, Examples 6, 8, 9, 10, 11, or 12). Furthermore, claims 33 and 34 have been amended to delete the word "therapeutically," to clarify that the pending claims are directed to methods of reducing colonization or shedding of EHEC and to avoid confusion with treatment or prevention of EHEC disease.

Therefore, the specification provides sufficient information to permit a reasonably skilled person (and as conceded by the Examiner, the relative skill of those in the art is high) to extrapolate the methods of the invention to a non-human mammal without undue

experimentation, and the test for enablement is fully satisfied. Accordingly, claims 33 and 34 are enabled. Since the remaining claims are dependent on claims 33 and 34 and by definition incorporate all the limitations of claims 33 and 34, the applicants respectfully submit that the dependent claims are also enabled. In this regard, the applicants also note that dependent claims 36 and 50 recite bovine subjects, which are stated as being enabled in the Office action, and that the enablement rejection therefore should not apply to these claims.

The applicants note that the Examiner's distinction between mammals that are carriers of EHEC (e.g., cattle) and those that are infected by EHEC (e.g., humans) is moot as the claims are now limited to "non-human" mammals. For the sake of completeness however the applicants respectfully submit that EHEC infection in humans does not necessarily preclude the ability of humans from also being carriers of EHEC. For example, the specification of the instant application, at paragraph 4, states that EHEC colonize the intestine of ruminants and other mammals. Furthermore, a publication by the Center for Food Security and Public Health at the Iowa State University College of Veterinary Medicine (enclosed herewith as "Exhibit A"), and reflecting the general knowledge regarding EHEC infections, states that a variety of animals, including humans, cattle, sheep, goats, pigs, etc. can be carriers of EHEC.

Claims 33-62 are rejected under 35 U.S.C. § 112, second paragraph, based on the assertion that they are indefinite. More specifically:

Claims 33 and 34 are rejected due to the lack of antecedent basis for "said ruminant." Claims 33 and 34 as presently amended recite "said non-human mammal" in place of "said ruminant" and therefore this rejection is moot.

Claims 43, 44, 57, and 58 are rejected as being indefinite for reciting the word "about." To expedite prosecution, these claims have been amended without prejudice to delete the word "about".

Claims 46, 48, 60, and 62 are rejected based on the assertion that the metes and bounds of the term "at least" is unclear. To expedite prosecution, these claims have been amended without prejudice to delete this term and to recite "10% to 50%" of the cell culture supernatant protein present in the composition. See paragraph [0096] of the published application for support.

Claims 45-48 and 59-62 are rejected for containing abbreviations. It is the applicant's understanding that the words "Tir," "EspA," "EspB," and "EspD" refer to the protein products of the corresponding genes "*tir*," "*espA*," "*espB*," and "*espD*" and are not abbreviations. Accordingly, the applicant respectfully submits that no correction is required.

Claims 42-44 and 56-58 are objected to for use of the term "VSA3" as being a trademark that had not been identified as such. This term has been deleted from these claims, and recited in new claim 81. As discussed herein, it is the applicant's understanding that the term VSA3 refers to an adjuvant formulation containing emulsion and dimethyldioctadecyl ammonium bromide (DDA) (see, for example, U.S. Patent 5,951,988 issued to Little-van den Hurk et al.) and is not a trademark. Accordingly, the applicant respectfully submits that the term "VSA3" does not require correction.

The applicants respectfully request that the Examiner not renew claim rejections under 35 U.S.C. § 112.

Rejection Under 35 U.S.C. § 102

Claims 33-36, 38, 45, 49, 50, and 59 are rejected under 35 U.S.C. § 102(a) as being anticipated by Li et al. (Infection and Immunity 68:5090, 2000; hereafter "Li"). More specifically, the Examiner asserts that Li teaches a method of reducing colonization of EHEC in a mammal by administering an EHEC cell culture supernatant. The Examiner also asserts that Li teaches reducing colonization in cattle and teaches EHEC 0157:H7, Tir, intimin, EspA, and EspB.

This rejection is respectfully traversed. Li does not constitute prior art in connection with the above-referenced patent application, as Li describes applicant Brett Finlay's own work, and was published less than one year before the effective filing date of January 4, 2001, of the above-referenced patent application. Enclosed herewith is the "Declaration of Dr. Brett Finlay" attesting to the fact that any description in Li was Dr. Finlay's sole contribution, notwithstanding the

inclusion of additional authors Yuling Li, Elizabeth Frey, and Andrew M. R. Mackenzie. More specifically, Yuling Li and Elizabeth Frey worked in Dr. Finlay's laboratory under his direction, and Andrew M. R. Mackenzie obtained and provided EHEC patient serum samples but did not otherwise contribute to the work described in Li. This Declaration is being submitted in accordance with 37 C.F.R. 1.131 and MPEP 715.01 (c) I.

Furthermore, for the sake of completeness the applicants respectfully submit that even if Li could be considered prior art, which it cannot, Li does not anticipate the claimed invention. Claims 33 and 34, which are the independent claims, are drawn to methods of reducing colonization or shedding, respectively, of EHEC in a non-human mammal by administering a composition that includes an EHEC cell culture supernatant. Claims 35, 36, 38, 45, 49, 50, and 59 depend from claim 33 or 34, and are therefore subject to all the limitations of claims 33 or 34. Accordingly, this rejection will be first addressed with respect to claims 33 and 34.

To support a rejection under § 102, a single prior art reference must describe each and every element, either expressly or inherently, of the rejected claims (MPEP § 2131), and Li does not meet this requirement. Li examines whether EHEC-infected human patients raise an immune response to specific EHEC virulence factors EspA, EspB, Tir, and intimin, by probing immunoblots of EHEC supernatants with sera taken from EHEC-infected patients, and makes a general suggestion that these specific virulence factors may be potential vaccine candidates, cautioning that additional studies need to be performed to evaluate the vaccine potential of these virulence factors. Li makes no mention of the possibility of administering an EHEC cell culture supernatant to a non-human mammal and does not describe a method of reducing colonization or shedding by administering a composition comprising an EHEC cell culture supernatant, as is asserted by the Examiner. Accordingly, since Li does not set forth each element and limitation of independent claims 33 and 34, and therefore of dependent claims 36, 38, 45, 49, 50, and 59, this rejection should be withdrawn.

Rejection Under 35 U.S.C. §103

Claims 33-62 are rejected under 35 U.S.C. § 103(a) as being *prima facie* obvious over Li

(*supra*) as applied to claims 33-36, 38, 45, 49, 50, and 59 and further in view of Little-Van den Hurk et al. (US Patent No. 5,951,988; hereafter "Little-Van den Hurk"). More specifically, the Examiner asserts that Li teaches a method of reducing colonization of EHEC in a mammal by administering an EHEC cell culture supernatant; teaches reducing colonization in cattle and teaches EHEC 0157:H7, Tir, intimin, EspA, and EspB. The Examiner also asserts that the '988 patent teaches adjuvants such as VSA3, and that the combination of Li and the '988 patent renders the claims obvious.

This rejection is respectfully traversed. To establish a *prima facie* case of obviousness, there must be a suggestion or motivation to combine or modify prior art reference(s); there must be a reasonable expectation of success; and the prior art references must teach or suggest all the claim limitations (MPEP § 2143). These criteria have not been met in the present case.

As indicated above in the section discussing the 35 U.S.C. § 102 rejection, Li does not constitute prior art. Furthermore, Li does not teach or suggest a method of reducing colonization or shedding in a non-human mammal by administering a composition comprising an EHEC cell culture supernatant, as is presently claimed. Little-Van den Hurk teaches adjuvant formulations containing quaternary ammonium salts in conjunction with an oil component and does not provide the requisite information, when combined with Li, that would teach or suggest that administering a composition including an EHEC cell culture supernatant would be effective in reducing colonization or shedding of EHEC. Thus, the combination of Li and Little-Van den Hurk does not meet any of the criteria required for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103, and this rejection should be withdrawn.

Conclusion

The applicants respectfully request that a timely Notice of Allowance be issued in this case.

Dated: September 1, 2004

Respectfully submitted,
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TMM:ct

"Exhibit A"

Escherichia coli 0157:H7 Infections

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Synonyms: Enterohemorrhagic *Escherichia coli* (EHEC), Verotoxin producing *Escherichia coli* (VTEC), Shiga toxin producing *Escherichia coli* (STEC)

Etiology

Escherichia coli 0157:H7 is a pathogenic, verotoxin-producing serotype of *E. coli.* This Gram negative motile rod belongs to the family Enterobacteriaceae and is responsible for many cases of hemorrhagic colitis in humans.

Geographic Distribution

Escherichia coli 0157:H7 infections occur worldwide.

Transmission

Transmission is by the fecal-oral route. Humans can be infected by direct contact with animal or human carriers; transmission by fomites, including water and food, is also common. Birds are potential vectors. Human outbreaks are often associated with eating improperly cooked or prepared animal products, particularly ground beef but also unpasteurized milk and processed meats (including acidic meats such as salami). Cider, alfalfa sprouts and other contaminated vegetable products have also been sources of epidemics.

Escherichia coli 0157:H7 remains viable for more than 2 months in feces and soil, and survives well in ground beef. It remains infectious for weeks to months in acidic foods such as mayonnaise, sausage, apple cider and cheddar at refrigeration temperatures. It is destroyed fairly quickly in slurry systems; in one experiment, organisms could no longer be recovered after 9 days.

Disinfection

E. coli 0157:H7 can be killed by numerous disinfectants including 1% sodium hypochlorite, 70% ethanol, phenolic or iodine-based disinfectants, glutaraldehyde and formaldehyde. It can be inactivated by moist heat (121° C for at least 15 min) or dry heat (160-170° C for at least 1 hour). Foods can be made safe by cooking them to a minimum temperature of 160°F/71°C. The infective dose is very low; washed vegetables may contain enough organisms to cause disease.

Infections in Humans

Incubation Period

The incubation period ranges from one to eight days in humans; one to two days is most common.

Clinical Signs

Human infection results in hemorrhagic colitis; this infection is characterized by cramps, abdominal pain, and watery diarrhea followed by bloody diarrhea. A low-grade fever may be present or absent in the

initial stages. Dehydration is possible. In healthy adults, infections are usually self-limiting and last about a week.

Serious complications can develop in a small percentage of cases. Hemolytic uremic syndrome (HUS) occurs in 2-10% of patients, usually a week after the diarrhea begins. HUS is characterized by kidney failure, which may result in permanent damage, and hemolytic anemia. Seizures, strokes, pancreatitis, colonic perforation, hypertension and coma may also be seen. Some patients develop permanent insulin-dependent diabetes. HUS can affect all ages but is most common in children under 10 years old.

Thrombotic thrombocytopenic purpura (TTP) is usually seen in adults, particularly the elderly. This disease resembles HUS and some sources consider it to be the same syndrome; there is typically less kidney damage but neurologic signs including stroke, seizures and CNS deterioration are more common.

Communicability
Yes, by the fecal oral route. Most people shed *E coli* 0157:H7 infections for approximately 7 to 9 days; a third of infected children can excrete this organism for as long as 3 weeks. Transmission is particularly common among children still in diapers.

Diagnostic Tests
E coli 0157:H7 infections are diagnosed by isolating the organism from fecal samples. This serotype is not detected in routine cultures but can be recognized by incubation on sorbitol-MacConkey agar. Antiserum can rapidly identify sorbitol-negative cultures as *E coli* 0157:H7. Fecal samples may be negative after one week. Another method of diagnosis is to test the feces for *E coli* verotoxin. Hemorrhagic colitis agar is used to isolate bacteria from food samples.

Treatment and Vaccination
Treatment of hemorrhagic colitis is supportive and may include fluids and a bland diet. Antibiotics are not typically used: they do not seem to reduce symptoms, prevent complications or decrease shedding and do appear to increase the risk of HUS. Patients with complications may require intensive care, including dialysis. Vaccines are not available.

Morbidity and Mortality
In the United States, approximately 73,000 infections are thought to occur yearly. Hemorrhagic colitis is generally self-limiting and illness usually lasts about a week. HUS develops in 2-10%. Complications and deaths are particularly common in young children, the elderly, and those with debilitating illnesses. HUS is fatal in 3-5% of patients and TTP in up to 50% of the elderly. Death can occur even in cases of uncomplicated colitis.

Infections in Animals
E. coli 0157:H7 has been found in cattle, sheep, goats, pigs, deer, dogs and poultry. The major reservoir of this organism is cattle; young animals are most likely to shed bacteria in the feces. Fecal shedding may last only weeks to months and can be intermittent.

Currently, there is no published evidence that *E coli* 0157:H7 causes disease in animals; however, B. Fenwick and colleagues have suggested that this organism may be linked to Idiopathic Cutaneous and Renal Glomerular Vasculopathy of Greyhounds (CRGV). Experimental infection of calves results in no clinical signs. Sheep also appear to carry the organism asymptomatically.

Internet Resources

Animal Health Australia. The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr-bin/aphb/ahsq?dislist=alpha

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/escherichiacoli_t.htm

Material Safety Data Sheets –Canadian Laboratory Center for Disease Control http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/index.html#menu

Medical Microbiology (textbook)
http://www.gsbs.utmb.edu/microbook

The Institute of Food Technologists
http://www.ift.org

The Merck Manual
http://www.merck.com/pubs/mmanual/

U.S. FDA Foodborne Pathogenic Microorganisms and Natural Toxins Handbook (Bad Bug Book)
http://vm.cfsan.fda.gov/~mow/intro.html

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